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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/513,888	02/25/2000	Carlo M. Croce	9855-30U1	6972

570 7590 06/03/2004

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2005 MARKET STREET, SUITE 2200
PHILADELPHIA, PA 19103-7013

EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/513,888	CROCE ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24 and 100-157* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23 and 24* is/are allowed.

6)☒ Claim(s) *100-157* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3-15-2004
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a response filed 3/15/2004 in which several new claims were added (new claims 145-157). Any rejection of record in this application not addressed herein is withdrawn. This action is FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 118-121, 141-142 and 144 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This rejection is maintained for reasons of record in the papers mailed 3/11/02 and 8/26/2003.**

Response to Arguments

Applicant's arguments filed 3/16/2004 have been fully considered but they are not persuasive. The responses essentially argue: 1) that each of the bases for traversal provided previously are incorporated by reference into the 3/16/2004 response, 2) the examiner has failed to provide any evidence underpinning his finding of facts and has not addressed each of applicants' rebuttal remarks (e.g. concerning the breadth of the claims), 3) the examiner has impermissibly declined to consider the references cited by applicants, 4) the initial references provided by the examiner cannot serve to demonstrate that all gene therapy is ineffective and

therefore cannot serve to show that the entire technology is unpredictable, 5) the level of the art is inextricably linked to the determination of whether any necessary experimentation is undue or routine, 6) when the level of a person of ordinary skill in the art is high both logic and law dictate that the level of complexity of experimentation may be greater.

To the extent that the 3/16/2004 response reiterates points argued previously, each of the examiner's responses and the original grounds of rejection are incorporated here by reference and are applicable as before. The examiner has provided rational argument and references to support such arguments concerning the level of success within the field of gene therapy. Assertions that the examiner did not fully consider the references provided by applicant in support of their argument concerning the enablement of the field of gene therapy are inaccurate and twist the examiner's comments out of context. Each of the references provided by applicants have been considered in full. For example, the references appear to point to some hope in the future for gene therapy applications, but there is no indication anywhere in the cited references concerning the applicability of the findings of those references to the claimed invention (i.e. FEZ1 activity). Further, at least two of the references are post-filing references that are not necessarily indicative of the state of the art at the time of the invention. With regard to the complexity of the invention, it is true that the level of skill in the art is inextricably tied to the analysis of the Wands factors. The examiner has considered this factor in context of all of the Wands factors and has determined that the high level of skill in the particular field of gene therapy does not in itself offset the problems of making practicing the claimed invention in a predictable manner that does not require undue experimentation.

Claims 100-157 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons of record in the papers mailed 3/11/02 and 8/26/2003. The grounds for rejection are extended to new claims 145-157. This is a NEW MATTER rejection.**

Response to Arguments

Applicant's arguments filed in the papers filed 3/16/2004 have been fully considered but they are not persuasive. The responses essentially argue: 1) the applicants were clearly in possession of the entire sequence of SEQ ID NO: 1 and, therefore, were clearly in possession of any subset of fragments, 2) the specification teaches that any of the fragments of SEQ ID NO: 1 can be used in the specification for any of the methods taught by the specification, 3) it is routine in the art to splice, truncate, snip and otherwise manipulate subsets of long sequences, and 4) the examiner is improperly applying the new matter principles related to ranges for example of temperature, etc., when the specification contains no disclosure of the intervening subsets whereas the instant specification teaches each an every nucleotide of SEQ ID NO: 1.

To the extent that the 3/16/2004 response reiterates points argued previously, each of the examiner's responses and the original grounds of rejection are incorporated here by reference and are applicable as before. While it is in fact routine to manipulate portions of a larger sequence in the art, this does not provide a literal basis for the recited limitations in the claims. The nucleotide sequence described by SEQ ID NO: 1 is over 9000 base pairs in length. Given

that applicants are reciting limitations for "portions" of SEQ ID NO: 1 that are variable in length, the number of different subsets of SEQ ID NO: 1 to choose from is nearly incalculable (e.g. every possible 20 nucleotide fragment over the entire 9 kb, plus every 21 nucleotide fragment available over the entire 9 kb, plus every 22 nucleotide fragment over the entire 9 kb, etc.). Thus, the assertion that it is not NEW MATTER to arbitrarily choose specific fragments from the extraordinarily broad genus of such fragments embraced by the rejected claims when the entire primary sequence is disclosed is inaccurate and unsupportable.

The argument concerning the misapplication of the new matter principles appears to be an assertion that each and every supposition of the larger sequence is functionally equivalent. First, there does not appear to be any legal finding to support applicants' assertion that the mere fact of providing each and every nucleotide within a larger sequence provides literal or inherent support for literally any sub portion of the larger sequence. Further, an assertion that there is no functional criticality to the endpoints is disingenuous at best. This appears to be an argument that all of the possible fragments of SEQ ID NO: 1 are functional equivalents to one another. If this is true, then it stands to reason that the fragments taught by, for example, Chader et al, make obvious all of the other possible fragments found within SEQ ID NO: 1. Applicants are attempting to have it both ways by claiming, on the one hand, that their invention is unique and novel of the prior art by arbitrarily choosing portions of SEQ ID NO: 1 to carve around the prior art while simultaneously claiming, on the other hand, there is nothing functionally important concerning the particular recited portions of SEQ ID NO: 1. Applicants have thus far failed to indicate where support can be found in the instant application for the specifically recited portions

of SEQ ID NO: 1 in the rejected claims. Therefore, the claims remain rejected on the basis of the introduction of impermissible NEW MATTER into the claims.

Claims 146-157 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by applicants' amendment of the claims in the response filed 3/16/2004.**

Each of the claims is directed to a polynucleotide encoding at least a portion of a polypeptide having particular functional activities (e.g. binding a fragment selected from the group of a fragment of tubulin or peptidomimetic of tubulin, EFI-γ, a peptidomimetic EFI-γ, a peptide that inhibits tubulin formation). The polynucleotide can comprise as few as 20 nucleotides or 100 nucleotides consecutive within SEQ ID NO: 1. The nucleotide sequence described by SEQ ID NO: 1 is over 9000 base pairs in length. Given that applicants are reciting limitations for "portions" of SEQ ID NO: 1 that are variable in length, the number of different subsets of SEQ ID NO: 1 to choose from is nearly incalculable (e.g. every possible 20 nucleotide fragment over the entire 9 kb, plus every 21 nucleotide fragment available over the entire 9 kb, plus every 22 nucleotide fragment over the entire 9 kb, etc.). Thus, the rejected claims comprise an enormous genus of polynucleotides that must also encode a peptide having very specific functional attributes.

The instant specification discloses the full-length coding sequence for FEZ1 (~9,000 base pairs). There does not, however, appear to be any significant teach with regard to which portions of SEQ ID NO: 1 encode a polypeptide having any of the specific functions recited in the rejected claims. The prior art does not appear to offset the deficiencies of the instant specification with regard to the recited functional activities and any particular peptide within the protein encoded by SEQ ID NO: 1.

Given the broad genus of polynucleotides encompassed by the rejected claims and the lack of any significant guidance from the specification and prior art concerning which of the regions within the protein encoded by SEQ ID NO: 1 that necessarily meet the functional limitations of the claims, the skilled artisan would not have been able to envision a sufficient number of specific embodiments of the claimed invention to describe the broadly claimed genus of polynucleotides. Therefore, the skilled artisan would reasonable have concluded applicants were not in possession of the claimed invention.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636

ggl

GERRY LEFFERS
PRIMARY EXAMINER